M. Pinkerton,

AMRL-TR-79-11
ADA Ø 672 13
Litation



ACUTE TOXICITY OF A NUMBER OF CHEMICALS OF INTEREST TO THE AIR FORCE

C. L. GAWORSKI E. R. KINKEAD R. L. DOYLE UNIVERSITY OF CALIFORNIA, IRVINE OVERLOOK BRANCH, P. O. BOX 3067 DAYTON, OHIO 45431

MARCH 1979

2003/202177

Approved for public release; distribution unlimited.

AEROSPACE MEDICAL RESEARCH LABORATORY
AEROSPACE MEDICAL DIVISION
AIR FORCE SYSTEMS COMMAND
WRIGHT-PATTERSON AIR FORCE BASE, OHIO 45433



NOTICES

When US Government drawings, specifications, or other data are used for any purpose other than a definitely related Government procurement operation, the Government thereby incurs no responsibility nor any obligation whatsoever, and the fact that the Government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data, is not to be regarded by implication or otherwise, as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto.

Please do not request copies of this report from Aerospace Medical Research Laboratory. Additional copies may be purchased from:

National Technical Information Service 5285 Port Royal Road Springfield, Virginia 22161

Federal Government agencies and their contractors registered with Defense Documentation Center should direct requests for copies of this report to:

Defense Documentation Center Cameron Station Alexandria, Virginia 22314

TECHNICAL REVIEW AND APPROVAL

AMRL-TR-79-11

The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council.

This report has been reviewed by the Information Office (OI) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

FOR THE COMMANDER

ANTHONY A. THOMAS, MD Director

Toxic Hazards Division

Aerospace Medical Research Laboratory

AIR FORCE/56780/28 March 1979 - 100

REPORT DOCUMENTATION	PAGE	READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
AMRL-TR-79-11		
4. TITLE (and Subtitle)		5. TYPE OF REPORT & PERIOD COVERED
ACUTE TOXICITY OF A NUMBER O	E CHEMICALS	
OF INTEREST TO THE AIR FORCE		
OF INTEREST TO THE AIR TORGE		6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s)		8. CONTRACT OR GRANT NUMBER(s) In part under Contract
C. L. Gaworski		F33615-76-C-5005
E. R. Kinkead		133010-10-0-0000
R. L. Doyle 9. PERFORMING ORGANIZATION NAME AND ADDRESS		10. PROGRAM ELEMENT, PROJECT, TASK
University of California, Ir	vine	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
Overlook Branch, P. O. Box 3		62202F, 6302 01 15
Dayton, Ohio 45431		•
11. CONTROLLING OFFICE NAME AND ADDRESS		12. REPORT DATE
Aerospace Medical Research Laborat	ory, Aerospace	March 1979
Medical Division, Air Force System		13. NUMBER OF PAGES
Wright-Patterson Air Force Base, C)hio 45433	32
14. MONITORING AGENCY NAME & ADDRESS(if different	from Controlling Office)	15. SECURITY CLASS. (of this report)
		UNCLASSIFIED
		15a. DECLASSIFICATION/DOWNGRADING
		SCHEDULE
Approved for public release;		
17. DISTRIBUTION STATEMENT (of the abstract entered in	n Block 20, 11 allierent tron	п кероті
18. SUPPLEMENTARY NOTES		·
·.		
		3
19. KEY WORDS (Continue on reverse side if necessary and		
	licyl Amino Gu	
		-Dimethylamino-p-Cresol
LD ₅₀ N,N'-Disalicylidene-1,2-Propane Diamine Skin Irritation 1,2,3-Benzotriazole		
3-Amino-1,2,4-Triazole Tricresyl Phosphate		
20. ABSTRACT (Continue on reverse side if necessary end identify by block number)		
A series of 20 chemical compounds used by the Air Force were		
evaluated for acute toxicity	y effects to ϵ	establish safe handling
		, irritation effects
and LD50 doses were determined for most of these materials. Of		
the compounds tested, nonyl phenol caused a skin sensitization		
reaction in 18 of 20 animals dosed and 1,4-dihydroxyanthraquinone which did not sensitize many animals, produced a very severe		
which did not sensitize many reaction in those affected.	y animais, pro	oduced a very severe
reaction in those affected.		

Block 19.

1,4-Dihydroxyanthraquinone
Sulfurized 9-Octadecenoic Acid
Azelaic Acid
Dimer Acid
N-Benzyl-3,7-Dioctyl Phenothiazine
Phenothiazine
Dioctyl Phenothiazine
Sebacic Acid
Acryloid HF-866
Acryloid HF-844
Guanidino Salicylamide Salt
Nonyl Phenol
Phosphonate Salt
Tris(β-Chloroethyl) Phosphate

PREFACE

This technical report describes results of acute toxicity tests on a number of Air Force materials. The work was performed by the University of California, Irvine, Department of Community and Environmental Medicine, Toxic Hazards Research Unit at Wright-Patterson Air Force Base, Ohio under Air Force Contract No. F33615-76-C-5005.

The current contract for operation of the Laboratory was initiated in 1975 under Project 6302 "Occupational and Environmental Toxic Hazards in Air Force Operations," Task 01 "Toxicology of Propellants and Materials", Work Unit Number 63020115. K. C. Back, Ph.D., Chief of the Toxicology Branch was the technical contract monitor for the Aerospace Medical Research Laboratory.

INTRODUCTION

Acute toxicity tests were performed on a number of commercial chemical materials being considered for technical use application by the United States Air Force. This group of 20 materials is identified in Table 1 together with the physical state. A preliminary search of the literature and manufacturers information failed to reveal any published documentation describing acute toxicity of these materials and it was, therefore, necessary to conduct a series of tests to evaluate the potential toxic hazard to personnel handling the materials.

Acute toxicity and irritation potentials were evaluated by using the following tests:

- 1. Single dose oral LD50 in rats and mice.
- 2. Primary skin irritation in rabbits.
- 3. Skin sensitization in guinea pigs.

Unfortunately, the supply of some of the materials was limited necessitating a prioritization of the tests performed.

TABLE 1. LIST OF AIR FORCE COMPOUNDS SUBMITTED FOR ACUTE TOXICITY STUDIES

Material and Physical State

3-amino-1,2,4-triazole (solid) Salicyl amino guanidine (liquid) 2,6-ditert-butyl-dimethylamino-p-cresol (solid) N, N'-disalicylidene-1, 2-propane diamine (liquid) 1,2,3-benzotriazole (solid) Tricresyl phosphate (liquid) 1.4-dihydroxyanthraquinone (solid) Sulfurized 9-octadecenoic acid (liquid) Azelaic acid (solid) Dimer acid (liquid) N-benzyl-3,7-dicotyl phenothiazine (solid) Phenothiazine (solid) Dioctyl phenothiazine (solid) Sebacic acid (solid) Acryloid HF-866 (liquid) Acryloid HF-844 (liquid) Guanidino salicylamide salt (liquid) Nonyl phenol (liquid) Phosphonate salt (liquid) Tris(β-chloroethyl)phosphate (liquid)

MATERIALS AND METHODS

ANIMALS

Male Sprague-Dawley rats weighing from 200 to 300 grams and male ICR mice weighing from 25-40 grams were obtained from Harlan Industries, Inc., for use in the LD50 determinations. Female New Zealand albino rabbits and male Hartley derived guinea pigs were obtained from Sweetwater Farms for use in the skin irritation and skin sensitization studies.

ACUTE ORAL TOXICITY - LD50 DETERMINATION

As a preliminary screen for the test materials, an oral dose of 5.0 g/kg body weight was administered to two rats. If no mortality occurred, the material was considered not to be toxic and no further oral toxicity tests were conducted. If mortality occurred, an oral LD50 was determined.

Solutions of the materials were prepared with corn oil or propylene glycol and administered in geometrically spaced doses using syringes and special oral dosing needles. Animals were fasted at least 16 hours prior to dosing to allow for a more uniform absorption of the material. Animals were weighed at the time of dosing to determine the proper dosing volume. For LD50 determinations, groups of five rats or mice were used per concentration. Animals were observed for 14 days after dosing. Any deaths occurring during this period were included in the final mortality results. The moving average interpolation method of Weil (1952) was used to determine the LD50 and 95% confidence limits. The following criteria, as published by Back et al. (1972), were used to classify the materials.

	Extremely <u>Toxic</u>	Highly <u>Toxic</u>	Toxic
Oral, 14-day	5 mg/kg or	>5-50	>50-5000
Single Dose LD50	less	mg/kg	mg/kg

PRIMARY SKIN IRRITATION

The primary skin irritation potential of the materials was measured by a patch test technique on intact and abraded skin areas of albino rabbits. Six rabbits were used for evaluation of each compound. The dorsal area of each rabbit was clipped free of hair 24 hours prior to administration of the compound, thus allowing irritation from the clipping process to heal. Equal numbers of exposures were made on the intact and abraded

Abrasions were minor incisions through the stratum corneum which were not deep enough to disturb the derma or to produce bleeding. The materials were applied in quantities of 0.5 grams for solids and 0.5 ml for liquids. Each site was covered with a 1 x 1 inch piece of surgical gauze two layers thick followed by a 4 x 4 inch piece of Elastoplast The entire area was covered with rubber dental adhesive tape. dam and secured with more Elastoplast tape. The rabbits were then fitted with leather restraining collars to prevent disturbance of the patch area. After 24 hours, the collars, dental dam, and patches were removed. Any reaction resulting from the test material was evaluated at this time and again at 72 hours post application using the method of Draize et al. (1959).

SKIN SENSITIZATION

Twenty male albino guinea pigs were used to test the sensitizing potential of the materials. The sensitization test was started on a Monday when the guinea pigs were weighed and closely clipped on the scapular areas. The material (0.05 ml of a 0.1% dilution in peanut oil) was injected intradermally into the upper right scapular area of each pig. A similar injection of peanut oil alone into the upper left scapular area served as a control site. Readings were made 24 and 48 hours later.

Doses of 0.1 ml of the same dilutions (freshly prepared) were injected into the clipped dorsal lumbo-sacral areas of the guinea pigs on the following Wednesday, Friday, Monday, etc., until seven doses were administered. Care was taken to insure that the repeated doses were not injected into the same site.

The guinea pigs were rested for three weeks (incubation period), weighed and given a challenge dose of 0.05 ml of the 0.1% dilution of the test material into the lower right scapular area. A control injection of the vehicle alone was also administered into the lower left scapular area at this time. The reactions were read after 24 and 48 hours.

The grading system is designed so that the intensity of the skin reaction is represented by a proportionate numerical value and also that any reaction elicited by the vehicle (control substance) is subtracted from the reaction elicited by the test material and vehicle combined.

The product of the width and length of the wheal (in mm) is multiplied by the following reaction scores to determine a final grade:

```
0 = needle puncture ("np") - no wheal
```

- 1 = very faint pink ("vfp") no value for this reaction
- 2 = faint pink ("fp")
- 3 = pink ("p")
- 4 = red ("r")
- 5 = bright red ("R")
- 6 = edema < 1 mm in height ("e")
- 7 = edema > 1 mm in height ("E")
- *8 = necrosis <1 sq. mm ("n")
- *9 = necrosis >1 sq. mm ("N")
- *The product of the width and length of the necrotic area multiplied by 8 or 9 is added to the numerical value of the foregoing reactions that are present and calculated in the same manner.

As a characterization of the sensitizing response which may be expected from exposure to the test material, the final grade was compared with the following categories.

<u>Final Grade</u>	Sensitizing Response	
0-25	None	
26-99	Mild	
100-200	Moderate	
>200	${ t Severe}$	

The sensitizing potential of the test material is estimated from the number of animals giving a response with a final grade of at least 25. The scale for this estimation is shown below:

Number Sensitized (N=20)	Sensitizing Potential	
1-3	Slight	
4-10	Moderate	
11-20	Severe	

RESULTS

The results of the acute oral toxicity data for the 21 materials tested are given in Table 2. Most of these chemical compounds are categorized as below toxic by this route of administration. When partial mortality or no deaths occur at the 5000 mg/kg dose level, no further testing is conducted since larger doses cannot be loaded into the gastrointestinal tract. With

guanidino salicylamide salt it was necessary to form a paste with corn oil and we were unable to give a large enough dose to cause any deaths in CF-1 mice. The rats used for oral dosing were Sprague-Dawley strain received from Carworth Farms.

TABLE 2. ACUTE ORAL TOXICITY OF AIR FORCE CHEMICALS

Compound	Species Male	LD ₅₀ (95% C.L.) in mg/kg	Data Used to Calculate LD $_{50}$ in mg/kg (Mortality Response, N = 2)	Classification
3-amino-1,2,4-triazole	Rat	>5000	5000(0)	Below Toxic
Salicyl amino guanidine	Rat	>5000	5000(0)	Below Toxic
2,6-ditert-butyl-di- methylamino-p-cresol	Rat ^a Mouse ^a	1189(669-2111) 307(190-496)	500(0),1000(3),2000(4) 125(0),250(2),500(4), 1000(5),2000(5)	Toxic Toxic
N,N'-disalicylidene- 1,2-propane diamine	\mathtt{Rat}^a Mouse b	2279(1344-3868)	1140(1),2280(2),4560(5)	Toxic
1,2,3-benzotriazole	Rat Mouse	1072(725-1585) 615(540-701)	500(0),1000(2),2000(5) 500(0),630(3),794(5)	Toxic Toxic
Tricresyl phosphate	Rat	>5000	5000(0)	Below Toxic
1,4-dihydroxyanthra- quinone	Rat	>5000	5000(0)	Below Toxic
Sulfurized 9-octa- decenoic acid	Rat	>5000	5000(0)	Below Toxic
Azelaic acid	Rat	>5000	5000(0)	Below Toxic
Dimer acid	Rat	>5000	5000(0)	Below Toxic
N-benzyl-3,7-dioctyl phenothiazine	Rat	>5000	5000(0)	Below Toxic
Phenothiazine	$\mathtt{Rat}^{a,b}$		5000(3)	
Dioctyl phenothiazine	Rat	>5000	5000(0)	Below Toxic
Sebacic acid	Rat	>5000	5000(0)	Below Toxic
Acryloid HF-866	Rat	>5000	5000(0)	Below Toxic
Acryloid HF-844	Rat	>5000	5000(0)	Below Toxic
Guanidino salicylamide salt	\mathtt{Rat}^b		5000(2)	Borderline Toxic
Nonyl phenol	Rat ^a Mouse ^a	2462(1788-3389) 1231(910-1665)	1000(0),2000(1),4000(5) 500(0),1000(1),2000(5) 4000(5)	Toxic Toxic
Phosphonate salt	Rat		5000(2)	10.110
Tris(β-chloroethyl) phosphate	Rat ^a	1131(499-2847)	200(0),400(0),800(0), 1600(3)	Toxic
abrive animals per level. Supply of the compound was 1	Mouse ^a	1866(1289-2701)	500(0),1000(0),2000(3), 4000(5)	Toxic

Supply of the compound was limited and used for other tests.

Only two of the compounds produced an irritation at the 24 or 72 hour readings. Salicyl amino guanidine treatment resulted in slight erythema and edema in three of the rabbits at 24 hours. Examination at 27 hours postexposure showed that the edema had generalized over the patch location and that five of the six rabbits had developed coriaceousness. One week after the exposure the "leathery" patches of skin had fissured and had begun to peel off. The primary irritation index score was determined to be 1.6, characteristic of mild irritation. However, the score is based upon edema and erythema results with necrotic development not being considered. In view of the tissue damage which resulted, the material should be considered a moderate to severe irritant.

Phosphonate salt produced slight erythema and edema at 24 hours. The edema had reduced at 72 hours, but the erythema was still present. The primary irritation index score was determined to be 2.4, thus classifying the material in the mild to moderate range.

All other compounds were found to be nonirritating at 24 and 72 hours postexposure examinations. Many of the liquid compounds apparently reacted with the adhesive of the patches and caused localized reactions. However, the reaction under the gauze patch was nil, thus the classification of nonirritating.

Skin sensitization and sensitization potential data were determined for Hartley strain guinea pigs. The results of these determinations on 17 compounds are presented in Table 3. The categorization of 1,4-dihydroxyanthraquinone as a compound with "slight" sensitization potential resulted when only two of the 20 guinea pigs tested reacted when given the challenge injection. The mean score for each of the two guinea pigs that reacted was over 800 which indicates a severe response. The mean for the entire group response diluted out the severity of this reaction and while only a small portion of any population might react to this material, the reaction for these individuals can be very intense. Special care should be taken in the handling of this compound to prevent skin contact and sensitization.

TABLE 3. SKIN SENSITIZATION TEST RESULTS ON 17 AIR FORCE MATERIALS DETERMINED IN GUINEA PIGS

Compound	Sensitization Response	Sensitization Potential
3-amino-1,2,4-triazole Salicyl amino guanidine	None Mild	None Moderate
2,6-ditert-buty1-dimethy1- amino-p-creso1	Mild	Slight
1,2,3-benzotriazole Tricresyl phosphate	Mild None	Slight None
1,4-dihydroxyanthraquinone Sulfurized 9-octadecenoic acid	Severe Mild	Slight Moderate
Azelaic acid Dimer acid	Mild None	Moderate None
N-benzyl-3,7-dioctyl phenothiazine	Mild	Slight
Phenothiazine	None	None
Dioctylphenothiazine Sebacic acid	Mild Mile	Moderate Slight
Acryloid HF-866 Acryloid HF-844 Nonyl phenol	Mild Mild Moderate	Slight Slight Severe
Tris(β-chloroethyl)phosphate	Moderate	Moderate

Nonyl phenol received a sensitization potential classification of severe since 18 of the 20 guinea pigs showed a reaction upon the challenge injection.

The sensitization tests were not conducted on three compounds, phosphonate salts, guanidino salicylamide salt and N,N'-disalicyldene-1,2-propane diamine because the supply of material available was exhausted in conducting other tests. Individual toxicity data sheets are presented in the Appendix of this report for each compound.

REFERENCES

Back, K. C., A. A. Thomas and J. D. MacEwen, (1972), <u>Reclassifi</u>-cation of Materials Listed as <u>Transportation Health Hazards</u>
<u>Report</u>, No. TSA 20-72-3, Department of <u>Transportation</u>.

Draize, J. H., (1959), "Dermal Toxicity," in Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics, The Staff of the Division of Pharmacology of the Federal Food and Drug Administration, Austin, Texas, The Editorial Committee of the Association of Food and Drug Officials of the United States, p. 51.

Weil, C. S., (1952), "Tables for Convenient Calculation of Median Effective Dose (LD $_{50}$ or ED $_{50}$) and Instructions in Their Use," Biometrics, 8:249-263.

APPENDIX

AIR FORCE MATERIALS

COMPOUND:

3-amino-1,2,4-triazole

1. ACUTE ORAL TOXICITY

R	ats	Mic	e
Dose (mg/kg)	Mortality <u>Ratio</u>	Dose (mg/kg)	Mortality Ratio
5000	0/2		

LD₅₀ (mg/kg): 95% C.L.:

>5000

LD50 (mg/kg): 95% C.L.:

Classification:

Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response

Sensitization Potential

None

None

COMPOUND: Salicyl amino guanidine

1. ACUTE ORAL TOXICITY

Rats		Mice		
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio	
5000	0/2			

LD₅₀ (mg/kg): >5000 95% C.L.: LD50 (mg/kg): 95% C.L.:

Classification: Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

Salicyl amino guanidine produced erythema and edema in 3 rabbits at 24 hours. Five of the 6 rabbits had developed oriaceousness at 72 hours. One week after application the "leathery" patches of skin had fissured and had begun to peel off. Irritation classified as severe.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response

Mild

Moderate

COMPOUND: 2,6-ditert-butyl-dimethylamino-p-cresol

1. ACUTE ORAL TOXICITY

Ra	ts	Mic	е
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
500 1000	0/5 3/5	125 250	0/5
2000	4/5	500 1000	2/5 4/5 5/5

LD₅₀ (mg/kg): 95% C.L.: LD50 (mg/kg): 95% C.L.: 1198 307

669-2111 190-496

Classification: Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response Sensitization Potential

> Mild Slight

COMPOUND: N, N'-disalicylidene-1, 2-propane diamine

ACUTE ORAL TOXICITY 1.

Ra	Rats <u>Mice</u>		e
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
1140	1/5	Not determ of limited	ined because supply.

LD₅₀ (mg/kg): 95% C.L.:

1344-3868

LD50 (mg/kg): 95% C.L.:

Classification: Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

SKIN SENSITIZATION - Guinea Pigs 3.

Sensitization Response

Not determined because of limited supply.

Sensitization Potential

Not determined because of limited supply.

COMPOUND: 1,2,3-benzotriazole

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose	Mortality	Dose (mg/kg)	Mortality
(mg/kg)	<u>Ratio</u>		Ratio
500	0/5	500	0/5
1000	2/5	630	3/5
2000	5/5	7 94	5/5

LD₅₀ (mg/kg): 1072 LD₅₀ (mg/kg): 615 95% C.L.: 725-1585 95% C.L.: 540-701

Classification: Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response

Mild

Slight

COMPOUND: Tricresyl phosphate

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
5000	0/2		

LD₅₀ (mg/kg): >5000 LD₅₀ (mg/kg): 95% C.L.:

Classification: Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response Sensitization Potential

None None

COMPOUND: 1,4-dihydroxyanthraquinone

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality <u>Ratio</u>	Dose (mg/kg)	Mortality Ratio
5000	0/2		

LD₅₀ (mg/kg): >5000 LD₅₀ (mg/kg): 95% C.L.: 95% C.L.:

Classification: Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response
Sensitization Potential
Severe
Slight

COMPOUND: Sulfurized 9-octadecenoic acid

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
5000	0/2		

LD₅₀ (mg/kg): >5000 LD₅₀ (mg/kg): 95% C.L.:

Classification: Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response

Mild

Moderate

COMPOUND: Azelaic acid

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
5000	0/2		

LD₅₀ (mg/kg): >5000 LD₅₀ (mg/kg): 95% C.L.: 95% C.L.:

Classification: Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits
No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

<u>Sensitization Response</u>

Mild

Moderate

COMPOUND:

Dimer Acid

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
5000	0/2		

LD₅₀ (mg/kg): 95% C.L.:

>5000

LD50 (mg/kg): 95% C.L.:

Classification:

Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

SKIN SENSITIZATION - Guinea Pigs 3.

Sensitization Response

Sensitization Potential

None

None

COMPOUND: N-benzyl-3,7-dioctyl phenothiazine

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
5000	0/2		•

LD₅₀ (mg/kg): >5000 LD₅₀ (mg/kg): 95% C.L.:

Classification: Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits
No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response

Mild

Slight

COMPOUND: Phenothiazine

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose	Mortality	Dose	Mortality
(mg/kg)	Ratio	(mg/kg)	Ratio

5000 . 3/5

Supply of the material was limited and used for other tests.

LD₅₀ (mg/kg): LD₅₀ (mg/kg): 95% C.L.: 95% C.L.:

Classification: Borderline Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response

None

Sensitization Potential

None

COMPOUND: Dioctyl phenothiazine

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
5000	0/2		

LD₅₀ (mg/kg): >5000 LD₅₀ (mg/kg): 95% C.L.: 95% C.L.:

Classification: Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response

Mild

Moderate

COMPOUND: Sebacic acid

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality <u>Ratio</u>	Dose (mg/kg)	Mortality Ratio
5000	0/2		

LD₅₀ (mg/kg): >5000 LD₅₀ (mg/kg): 95% C.L.: 95% C.L.:

Classification: Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response

Mild

Slight

COMPOUND:

Acryloid HF-866

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
5000	0/2		•

LD₅₀ (mg/kg): 95% C.L.: >5000

LD50 (mg/kg): 95% C.L.:

Classification:

Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

SKIN SENSITIZATION - Guinea Pigs 3.

Sensitization Response

Sensitization Potential

Mild

Slight

COMPOUND: Acryloid HF-844

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
5000	0/2		

LD₅₀ (mg/kg): >5000 LD₅₀ (mg/kg): 95% C.L.:

Classification: Below Toxic

2. PRIMARY SKIN IRRITATION - Rabbits
No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response

Mild

Slight

COMPOUND: Guanidino salicylamide salt

1. ACUTE ORAL TOXICITY

Rats		${ t Mice}$	
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
5000	1/2		•

Supply of the material was limited and used for other tests.

LD₅₀ (mg/kg): LD₅₀ (mg/kg): 95% C.L.: 95% C.L.:

Classification: Borderline Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

<u>Sensitization Response</u> Not determined because of limited supply. Sensitization Potential Not determined because of limited supply.

Nonyl phenol COMPOUND:

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality Ratio	Dose (mg/kg)	Mortality Ratio
1000	0/5	500	0/5
2000	1/5	1000	1/5
4000	5/5	2000	5/5
	•	4000	5/5

1231

LD₅₀ (mg/kg): 2462 95% C.L.: 1788-3 LD50 (mg/kg): 95% C.L.: 1788-3389 910-1665

Classification: Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

SKIN SENSITIZATION - Guinea Pigs 3.

Sensitization Response Sensitization Potential Moderate Severe

COMPOUND: Phosphonate salt

1. ACUTE ORAL TOXICITY

Rats		Mice	
Dose (mg/kg)	Mortality <u>Ratio</u>	Dose (mg/kg)	Mortality Ratio
5000	2/5		

Supply of the material was limited and used for other tests.

LD₅₀ (mg/kg): LD₅₀ (mg/kg): 95% C.L.: 95% C.L.:

Classification: Borderline Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

Phosphonate salt produced slight erythema and edema at 24 hours. Irritation classified as mild.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response	Sensitization Potential
Not determined because of limited supply.	Not determined because of limited supply.

COMPOUND: Tris(β-chloroethyl)phosphate

ACUTE ORAL TOXICITY 1.

Rats		Mice	
Dose	Mortality	Dose (mg/kg)	Mortality
(mg/kg)	<u>Ratio</u>		Ratio
200	0/5	500	0/5
400	0/5	1000	0/5
800	0/5	2000	3/5
1600	3/5	4000	5/5

1131 1866

LD₅₀ (mg/kg): 95% C.L.: LD50 (mg/kg): 95% C.L.: 499-2847 1289-2701

Classification: Toxic

2. PRIMARY SKIN IRRITATION - Rabbits

No irritation.

3. SKIN SENSITIZATION - Guinea Pigs

Sensitization Response Sensitization Potential

Moderate Moderate